REMARKS

The requisite fee of $120.00 for a one-month extension of time may be charged to Deposit Account No. 02-1818. Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 02-1818. If a Petition for Extension of Time is needed, this paper is to be considered such Petition.

Claims 1-52, 54-84, 86-136 and 138 are pending. Claim 138 is added and claims 3, 6, 9, 12, 15, 17, 19, 25, 31, 32, 50, 70, 121, 132 and 134 are amended herein. Claims 3, 6, 9, 12, 15, 17, 19, 25, 31, 32 and 50 are amended to correct antecedent basis of terms recited therein. Claims 3 and 6 are amended to replace the recitation "halo" in the definition of substituent R_2 with the recitation "F, Cl Br," antecedent basis for which is found in claim 1, which recites "R_2 is selected from among hydrogen, F, Cl, Br, ..." Claims 6 and 12 are amended to replace the recitation "halo" in the definition of substituent R_3 with the recitation "F, Cl Br," antecedent basis for which is found in claim 1, which recites "R_3 is selected from among hydrogen, F, Cl, Br, ..." Claim 15 is amended to replace the recitation "halo" in the definition of substituent R_4 with the recitation "F, Cl Br," and claims 17 and 19 are amended to replace the recitation "halogen" in the definition of substituent R_4 with the recitation "F, Cl Br," antecedent basis for which is found in claim 1, which recites "R_4 is selected from among hydrogen, F, Cl, Br, ..." Claim 25 is amended to replace the recitation "halo" with the recitation "F, Cl Br," antecedent basis for which is found in claim 1, which recites "R_5 is selected from among hydrogen, F, Cl, Br, ..." Claims 31 and 32 are amended to replace the recitation "halo" with the recitation "F, Cl Br," antecedent basis for which is found in claim 1, which recites "R_6 is selected from among hydrogen, F, Cl, Br, ..." Claim 50 is amended to replace the recitation "halogen" with the recitation "F, Cl Br," antecedent basis for which is found in claim 1, which recites "R_7 is selected from among hydrogen, F, Cl, Br, ..." Claims 70, 121, 132 and 134 are amended to correct typographical or formatting errors. Basis for new claim 138 can be found, *e.g.*, at page 58, lines 18-9. No new matter is added.

TRAVERSAL OF THE FINDING OF LACK OF UNITY

The Office Action restricts the pending claims into four groups as follows:

Group I: Claims 1-120, 126-131, drawn to compounds;
Group II: Claim 121, drawn to articles of manufacture;
Group III: Claims 122-125, 134-136, drawn to method of treating, preventing, or ameliorating the symptoms or manifestation of a disease or disorder that is modulated by or otherwise affected by glucocorticoid receptor activity; and
Group IV: Claims 132 and 133, drawn to a method for identifying a compound capable of modulating an activity of a glucocorticoid receptor.

The Examiner, recognizing that the rules of unity of invention under PCT Rule 13.1 apply to the instant case, urges that there is a lack of unity because the four groups allegedly do not relate to a single inventive concept. This conclusion is based upon the premise that a special technical feature between the groups is disclosed in Coghlan *et al.* (WO 02/02565, published 10 January 2002).

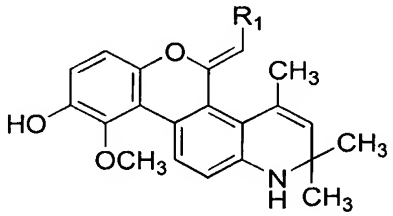
The Examiner alleges that the common technical feature among the claims is a compound of Formula I. The Office Action alleges that the claims of Groups I - IV lack unity of invention because the compound of claim 1 allegedly is not novel. The Examiner alleges that Coghlan *et al.* discloses a compound on page 36, lines 20-21 having a structure of Formula I where R_1 is Formula II and R_2-R_6 are hydrogen and therefore allegedly destroys novelty of the compounds of claim 1 and unity of invention amongst groups I-IV.

Reconsideration of the finding of a lack of unity and withdrawal of the Restriction Requirement respectfully are requested in view of the following remarks. The compound of claim 1, as discussed below, is novel over the cited art, rendering it a novel technical feature shared among all pending claims. Therefore, all pending claims are unified.

The Claims

Claim 1 of Group 1 recites:

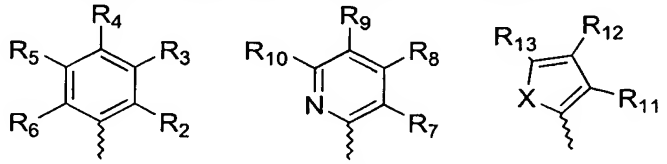
A compound of Formula I:



(I)

or a pharmaceutically acceptable derivative thereof, wherein:

R_1 is selected from among Formula II, III, and IV:



(II) ***(III)*** ***(IV)***

R_2 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, -$CONR_{14}R_{15}$, -OR_{16}, -COR_{16}, -SR_{16}, -$SO_2NR_{14}R_{15}$, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

R_3 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally

substituted haloalkyl, an optionally substituted heteroalkyl, -OR_{16}, -SR_{16}, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

R_4 is selected from among hydrogen, F, Cl, Br, CN, -OR_{16}, -SR_{16}, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl; or

R_2 and R_3 together form an optionally substituted 5-6 member ring and R_4 is selected from among hydrogen, F, Cl, Br, CN, -OR_{16}, -SR_{16}, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl; or

R_3 and R_4 together form an optionally substituted 4-6 member ring and R_2 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, -$CONR_{14}R_{15}$, -OR_{16}, -SR_{16}, -$SO_2NR_{14}R_{15}$, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

R_5 is selected from among hydrogen, F, Cl, Br, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, -SR_{16} and -OR_{16};

R_6 is selected from among hydrogen, F, Cl, Br, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl;

R_7 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, -$CONR_{14}R_{15}$, -$SO_2NR_{14}R_{15}$, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

R_8 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, -OR_{16}, -SR_{16}, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

R_9 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, and an optionally substituted heteroalkyl; or

R_7 and R_8 together form an optionally substituted 5-6 member ring and R_9 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, and an optionally substituted heteroalkyl; or

R_8 and R_9 together form an optionally substituted 4-6 member ring and R_7 is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, -$CONR_{14}R_{15}$, and an optionally substituted aryl;

R_{10} is selected from among hydrogen, F, Cl, Br, an optionally substituted alkyl, an optionally substituted alkenyl, and an optionally substituted alkynyl; and

R_{11} is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, hydroxyiminoalkyl, alkoxyiminoalkyl, aryloxyiminoalkyl, -$CONR_{14}R_{15}$, $SO_2NR_{14}R_{15}$, OR_{16}, -SR_{16}, -COR_{16}, an

optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

R_{12} is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, -OR_{16}, -SR_{16}, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

R_{13} is selected from among hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, and an optionally substituted heteroalkyl; or

R_{11} and R_{12} together form an optionally substituted 5-6 member ring and R_{13} is selected from among hydrogen, F, Cl, Br, CN, $CONR_{14}R_{15}$, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, and an optionally substituted heteroalkyl; or

R_{12} and R_{13} together form an optionally substituted 4-6 member ring and R_{11} is selected from among hydrogen, F, Cl, Br, CN, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, -$CONR_{14}R_{15}$, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

R_{14} and R_{15} are each independently selected from among hydrogen, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted cycloalkyl and an optionally substituted heteroalkyl; or

R_{14} and R_{15} together form an optionally substituted 4-7 member ring;

R_{16} is selected from among hydrogen, an optionally substituted alkyl, an optionally substituted alkenyl, an optionally substituted alkynyl, an optionally substituted haloalkyl, an optionally substituted heteroalkyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl and an optionally substituted cycloalkyl;

X is selected from among O, S, and NR_{17}; and

R_{17} is selected from among hydrogen, an optionally substituted alkyl, an optionally substituted alkenyl and an optionally substituted alkynyl;

wherein the substituents on the alkyl, alkenyl, alkynyl, aralkyl, aryl, heteroaryl, heterocyclyl, and cycloalkyl groups, when present, are each individually and independently selected from one to four group(s) selected from among: alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, non-aromatic heterocycle, hydroxy, alkoxy, alkoxyalkoxy, aryloxy, mercapto, alkylthio, arylthio, cyano, halo, carbonyl, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyiminothiocarbonyl, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, C-amido, N-amido, S-sulfonamido, N-sulfonamido, C-carboxy, O-carboxy, isocyanato, thiocyanato, isothiocyanato, nitro, silyl, trihalomethanesulfonyl, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylamino-carbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy and amino; including mono- and di-substituted amino groups, and the protected derivatives of amino groups;

wherein at least one position selected from among R_2, R_3, R_4, R_5, and R_6 is not hydrogen;

at least one position selected from among R_7, R_8, R_9, and R_{10} is not hydrogen;

if R_4 is F, then at least one position selected from among R_2, R_3, R_5 and R_6 is not hydrogen;

if R_3 is F, then at least one position selected from among R_2, R_4, R_5, and R_6 is not hydrogen; and

if any two positions selected from among R_2, R_3, R_4, R_5, and R_6 are both F, then at least one of the other three positions selected from R_2, R_3, R_4, R_5, and R_6 is not hydrogen.

The claim of Group II is directed to an article of manufacture that includes a a compound of claims of Group I.

The claims of Group III are directed to methods treating, preventing, or ameliorating the symptoms or manifestation of a disease or disorder that is modulated by or otherwise affected by glucocorticoid receptor activity, where the methods include as a step administration of a compound of claims of Group I.

The claims of Group IV are directed to a method for identifying a compound that modulates an activity of a glucocorticoid receptor using a compound of claims of Group I.

Hence, a compound of claim 1 is a technical feature shared among all pending claims. As discussed below, it respectfully is submitted that the compounds of claim 1 are novel over the cited art. Therefore, all pending claims are unified.

Disclosure of the Cited Art

Coghlan *et al.* discloses benzopyrano[3,4-*f*]quinolines as glucocorticoid-selective anti-inflammatory agents. Among the compounds disclosed in Coghlan *et al.* are compounds that include a benzylidene moiety, such as Example 365 (which has an unsubstituted benzylidene ring), Example 366 (which has a benzylidene ring substituted at positions 2 and 5 with F) and Example 374 (which has a benzylidene ring substituted at position 3 with F).

Coghlan *et al.* does not disclose any compound that includes a benzylidene ring substituted at position 3 with F that is substituted with a substituent other than hydrogen at at least one other position of the benzylidene ring. Coghlan *et al.* does not disclose any compound that includes a benzylidene ring substituted at any two of positions 2, 3, 4, 5 and 6 with F, where at least one of the other three positions of the benzylidene ring is a substituent other than hydrogen.

Analysis

A common underlying technical feature among the claims of Groups I-IV is a compound of Formula I as described in claim 1, which recites that at least one position selected from among R_2, R_3, R_4, R_5, and R_6 is not hydrogen, that if R_3 is F, then at least one position selected from among R_2, R_4, R_5, and R_6 is not hydrogen and that if any two positions selected from among R_2, R_3, R_4, R_5, and R_6 are both F, then at least one of the other three

positions selected from R_2, R_3, R_4, R_5, and R_6 is not hydrogen. In order for Coghlan *et al.* to destroy unity among Groups I-IV, Coghlan *et al.* must disclose a compound that includes every element of the instant claims.

The compound cited by the Examiner at page 36, lines 20-21 of Coghlan *et al.* is Z-5-(benzylidenyl)-9-hydroxy-10-methoxy-2,2,4-trimethyl-1*H*-2,5-dihydro-[1]benzopyrano[3,4-*f*]-quinoline. The compound includes an unsubstituted benzylidene ring, which corresponds to a compound of instant Formula I where R_1 is Formula II and each of R_2-R_6 is hydrogen. Claim 1 recites at least one position selected from among R_2, R_3, R_4, R_5 and R_6 is not hydrogen. Because the compound cited by the Examiner has a hydrogen at each of positions R_2, R_3, R_4, R_5 and R_6 , the cited compound is not within the scope of the instant claims and thus does not destroy novelty.

Coghlan *et al.* discloses other compounds containing a benzylidene moiety, such as the compounds described in Examples 366 and 374. The compound of Example 366 of Coghlan *et al.* is Z-5-(2,5-difluorobenzylidene)-9-hydroxy-10-methoxy-2,2,4-trimethyl-1*H*-2,5-dihydro-[1]benzopyrano[3,4-*f*]quinoline. This compound includes a benzylidene ring substituted at positions 2 and 5 with fluorine. Positions 3, 4 and 6 of the benzylidene ring are unsubstituted. Instant claim 1 recites that if any two positions selected from among R_2, R_3, R_4, R_5, and R_6 are both F, then at least one of the other three positions selected from R_2, R_3, R_4, R_5, and R_6 is not hydrogen. Because the compound of Example 366 of Coghlan *et al.* is substituted with F at positions 2 and 5 (corresponding to R_2 and R_5 of the instant claims) and each of the positions 3, 4 and 6 (corresponding to R_3, R_4 and R_6 of the instant claims) has hydrogen as the only substituent, the compound of Example 366 of Coghlan *et al.* is not within the scope of the instant claims and thus does not destroy novelty.

The compound of Example 374 of Coghlan *et al.* is Z-5-(3-fluorobenzylidene)-10-methoxy-9-hydroxy-2,2,4-trimethyl-2,5-dihydro-1*H*-benzopyrano [3,4-*f*]quinoline. This compound includes a benzylidene ring substituted at position 3 with fluorine. Positions 2, 4, 5 and 6 of the benzylidene ring are unsubstituted. Instant claim 1 recites that if R_3 is F, then at least one position selected from among R_2, R_4, R_5, and R_6 is not hydrogen. Because the compound of Example 374 of Coghlan *et al.* is substituted with F at position 3 (corresponding to R_3 of the instant claims) and each of positions 2, 4, 5 and 6 (corresponding to R_2, R_4, R_5 and R_6 of the instant claims) is hydrogen, the compound of Example 374 of Coghlan *et al.* is not within the scope of the instant claims and thus does not destroy novelty.

None of the compounds disclosed in Coghlan *et al.*, such as the compounds described in Examples 365, 366 and 374, includes every element of claim 1. Thus, Coghlan *et al.* does not anticipate the compounds of claim 1. Therefore, Coghlan *et al.* does not destroy novelty of the compounds of claim 1. A compound of claim 1 is a technical feature shared among all claims of Groups I-IV. Thus, Groups I-IV (claims 1-52, 54-84, 86-136 and 138) possess unity. Therefore, the claims of Groups II-V should be rejoined with the claims of Group I and examined in this application.

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In view of the election, amendments and remarks herein, withdrawal of the restriction requirement, examination on the merits and allowance respectfully are requested.

Respectfully submitted,

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